

An Indian-Australian research partnership

<b>Project Title:</b>	<b>Engineering advanced enzyme biocatalysts for synthesis of chiral drug intermediates</b>	
<b>Project Number</b>	IMURA0334	
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## Research Academy Themes:

**Highlight which of the Academy's Theme(s) this project will address?**

*(Feel free to nominate more than one. For more information, see [www.iitbmonash.org](http://www.iitbmonash.org))*

5. Nanotechnology
6. Biotechnology and Stem Cell Research

## The research problem

*Define the problem*

Enzymes are currently ubiquitously deployed in processes and products ranging from food and chemical processing to bio-energy and water treatment. Enzymatic approaches have also been finding increased acceptance in the fine chemicals and pharmaceutical industry, given that they facilitate the synthesis of several intermediates using green and industrially inexpensive reaction conditions. The annual global market for industrial enzymes grew at a near double digit pace, and increased from \$2 bn in 2000 to \$5.1 bn in 2009.

One attractive application of enzymes is in the synthesis of chiral drug intermediates. Enantiomerically pure or enriched organic compounds are highly desirable in the pharmaceutical industry. Classical chemical synthesis routes produce racemic mixtures of enantiomers; subsequent separation of the desired enantiomer can then be expensive. The problem of racemic mixtures can be resolved using enzymes to facilitate kinetic resolution towards a high enantioselectivity. For instance, lipases have found widespread use for the preparation of optically pure compounds and processes where chemoselectivity and regioselectivity are important. They have several process advantages: they are stable in organic solvents, have a broad substrate

spectrum, work under mild reaction conditions, and do not need addition of cofactors.

However, enzymes are often expensive to recover and deploy. Different approaches have been used to enhance enzyme functions while decreasing their production cost. These include using new microbial hosts for enzyme production, screening technologies such as directed evolution to determine better enzymes, computational design for recombinant enzymes, and chemical and engineering methods such as enzyme immobilisation to facilitate catalyst reusability.

Large scale deployment of enzymes remains confined to a few pharmaceutical processes and poses several process challenges. *These challenges require a multidisciplinary approach to simultaneously realize high performance and low cost for creation of advanced biocatalysts.*

## Project aims

*Define the aims of the project*

The **goal of this project** is to discover new knowledge and methods for designing and engineering biocatalysts with high performance at low cost. A specific objective is to develop lipases that have high specificity and activity for synthesis of specific chiral drug intermediates. New strategies will be developed to immobilize lipase onto silica nanoparticles towards improving enzyme stability and re-usability. The project will also standardize production methods for synthesis of lipase using engineered expression systems. This research will deliver fundamental understanding of physicochemical properties of engineered enzymes to enable **clearer molecular design and engineering rules for a new generation of enzymes as better and sustainable biocatalysts**. The project aims to

- (a) engineer enzymes with better activity and selectivity for synthesis of chiral drug intermediates;*
- (b) develop new immobilization strategies to achieve excellent immobilization while also ensuring immobilization can be carried out cost effectively;*
- (c) develop bioprocesses that can be used to make enzymes cheaply and quickly; and*
- (d) establish design rules for rational manufacture and deployment of immobilized biocatalysts.*

## Expected outcomes

*Highlight the expected outcomes of the project*

This research is expected to result in innovative science and engineering outcomes leading to identification of advanced enzyme biocatalysts which can be used for synthesis of chiral drug intermediates.

Expected research outcomes will include:

- engineered new lipase that has a better activity and selectivity for synthesis chiral drug intermediates;*
- new immobilization strategies that can achieve excellent immobilization while also ensuring cost-effective immobilization*
- new bioprocesses that can be used to make enzymes cheaply and quickly;*
- design rule to make better lipase-biocatalysts.*

## How will the project address the Goals of the above Themes?

*Describe how the project will address the goals of one or more of the 6 Themes listed above.*

This proposed research is a multidisciplinary effort which would seek to combining nanotechnology and biotechnology methods to develop advanced biocatalysts which can be used for synthesis of chiral drug intermediates. It will address two goals of the 6 themes of the research academy as follows:

### *Goal 6: Biotechnology and Stem Cell Research*

- 1) Immobilized enzymes with better activity and selectivity for synthesis of chiral drugs will be identified.
- 2) Cheap, scalable approaches for synthesis and deployment of biocatalysts will be developed.

### *Goal 5: Nanotechnology*

Nanotechnology will play an important role in this project, specifically for enzyme immobilization. This will comprise four components including nanoparticle synthesis, functionalization of nanoparticles, enzyme immobilization and activity analysis of the immobilized enzymes. Silica nanoparticles with different particle and pore sizes will be prepared using new methods in order to investigate how these two key physical properties affect enzyme immobilization efficiency, enzyme activity, and selectivity.

## Capabilities and Degrees Required

*List the ideal set of capabilities that a student should have for this project. Feel free to be as specific or as general as you like. These capabilities will be input into the online application form and students who opt for this project will be required to show that they can demonstrate these capabilities.*

- M.Sc., or M.Tech Biochemistry or Biotechnology or equivalent. Project-related experience with biochemistry, microbiology and molecular biology techniques would be an advantage.
- Chemical engineering background with project experience related to microbial biotechnology.